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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/117,246	12/03/1998	DOLORES LUDEVID	50062/004001	3466

21559 7590 05/17/2006

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EXAMINER
KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 05/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/117,246	LUDEVID ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,43,45,46,51,56,65-68,76 and 84-124* is/are pending in the application.

4a) Of the above claim(s) *51,56,65-68 and 76* is/are withdrawn from consideration.

5)☒ Claim(s) *124* is/are allowed.

6)☒ Claim(s) *42,43,45,46 and 84-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *attachement #1*.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/18/2005 has been entered.

Claims 1-41, 44, 47-50, 52-55, 57-64, 69-75 and 77-83 are cancelled. Claims 42-43, 45-46, 51, 56, 65-68, 76 and 84-124 are pending. Claims 51, 56, 65-68 and 76 are withdrawn. Claims 42-43, 45-46 and 84-124 are examined.

Rejection of Claims 47-50, 52-55, 57-63, 69-75 and 77-83 under 35 U.S.C. 112, first paragraph, NEW MATTER is withdrawn in view of Applicant's amendments.

Rejection of Claims 42-43 and 45-46 under 35 U.S.C. 102(b) is withdrawn in view of Applicant's amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-43, 45, 84-88, 110-114, 116-120 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 4/20/2004 and 10/12/2004. Applicant's arguments filed 9/23/2004 and 10/18/2005 have been considered but are not deemed persuasive.

Applicant broadly claims broadly claimed genus of polynucleotides encoding plant reserve proteins having P-K concantenations or oligonucleotides of wherein 'n' is 2 or more or 3 or greater having no upper limit or no limit to the size of non P-K intervening regions and unspecified with respect to the placement within the unspecified reserve protein comprising any number of concantenations; and maize seeds comprising said unspecified reserve proteins.

Applicant describes polynucleotides encoding 28kDa gamma zein from maize comprising high lysine modifications as P20γZ (SEQ ID NO: 11) having K-(P-K)$_4$ (SEQ ID NO: 3) inserted after the Pro-X domain, H30γZ (SEQ ID NO: 7) having K-(P-K)$_4$ (SEQ ID NO: 3) replacing the Pro-X domain, H45γZ (SEQ ID NO: 9) having K-(P-K)$_4$-E-F-K-(P-K)$_4$ (SEQ ID NO: 4) replacing the Pro-X domain and pN13γZ having SEQ ID NO: 5 inserted 5 amino acid residues upstream of the carboxy terminus of the peptide (see Figure 3).

Applicant does not describe any other concantenations of P-K in any other plant storage proteins other than those of the modified gamma zein from maize comprising high lysine modifications as P20γZ (SEQ ID NO: 11) having K-(P-K)$_4$ (SEQ ID NO: 3) inserted after the Pro-X domain, H30γZ (SEQ ID NO: 7) having K-(P-K)$_4$ (SEQ ID NO: 3) replacing the Pro-X

domain, H45γZ (SEQ ID NO: 9) having K-(P-K)$_4$-E-F-K-(P-K)$_4$ (SEQ ID NO: 4) replacing the Pro-X domain and pN13γZ having SEQ ID NO: 5 inserted 5 amino acid residues upstream of the carboxy terminus of the peptide (see Figure 3)

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences encoding a plant reserve protein comprising a P-K concantenation falling within the scope of the claimed genus of polynucleotides encoding plant reserve proteins comprising any number of P-K concantenations.

Applicants only describe SEQ ID NO: 6, 8 and 10 encoding SEQ ID NO: 7, 9 and 11. Furthermore, Applicants fail to describe structural features common to members of the broadly claimed genus of polynucleotides encoding plant reserve proteins having P-K concantenations or oligonucleotides comprising any number of concantenations having no upper limit or no limit to the size of non P-K intervening regions. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary placement of the P-K concantenations for either storage preteins or oligonucleotides encoding a polypeptide, it remains unclear what features identify polynucleotide encoding a reserve protein or an oligonucleotide encoding a protein having P-K concantenations. Since the genus of

polynucleotides encoding plant reserve proteins modified to have any number of P-K concantenations or the oligonucleotides has not been described by specific structural features or modification sites, the specification fails to provide an adequate written description to support the breath of the claims.

Sequences encoding plant reserve proteins having P-K concantenations encompasses naturally occurring allelic variants, mutants, as well as sequences encoding proteins having no known function of which Applicant is not in possession. Accordingly, the specification fails to provide an adequate written description to support the genus of polynucleotides encompassed by the language as set forth in the claims. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

Applicant asserts that new claims 114-123 are limited to maize seeds and thus have overcome any rejection under 112 1st written description (response page 19). Applicant has not presented the structure of any other protein comprising the oligonucleotide of the invention other than the modified maize gamma zein. Clearly from Applicant's specification the placement of the P-K regions in the gamma zein are critical for stability or activity in the seed of maize and one of skill in the art would require an adequate description of the relative placement of P-K conacantamers as well as size of said concantemers and any intervening regions as well for the non-described reserve proteins that do not share the same structural elements of the maize gamma zein (28kDa).

Claims 42-43, 45, 84-88, 110-114, 116-120 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Maize transformed with the modified gamma zein from maize comprising high lysine modifications as P20γZ (SEQ ID NO: 11) having K-(P-K)$_4$ (SEQ ID NO: 3) inserted after the Pro-X domain, H30γZ (SEQ ID NO: 7) having K-(P-K)$_4$ (SEQ ID NO: 3) replacing the Pro-X domain, H45γZ (SEQ ID NO: 9) having K-(P-K)$_4$-E-F-K-(P-K)$_4$ (SEQ ID NO: 4) replacing the Pro-X domain and seeds thereof and methods therewith, does not reasonably provide enablement for any plant transformed with a modified maize gamma zein stably expressing any plant reserve protein or any reserve protein plant or otherwise stably expressed in the seeds of a plant other than the modified gamma zein from maize comprising high lysine modifications as P20γZ (SEQ ID NO: 11) having K-(P-K)$_4$ (SEQ ID NO: 3) inserted after the Pro-X domain, H30γZ (SEQ ID NO: 7) having K-(P-K)$_4$ (SEQ ID NO: 3) replacing the Pro-X domain, H45γZ (SEQ ID NO: 9) having K-(P-K)$_4$-E-F-K-(P-K)$_4$ (SEQ ID NO: 4) replacing the Pro-X domain in the seeds of maize. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official action mailed 4/20/2004 and 10/12/2004. Applicant's arguments filed 9/23/2004 and 10/18/2005 have been considered but are not deemed persuasive.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of

experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicant broadly claims broadly claimed genus of polynucleotides encoding plant reserve proteins having P-K concantenations or oligonucleotides of wherein 'n' is 2 or more or 3 or greater having no upper limit or no limit to the size of non P-K intervening regions and unspecified with respect to the placement within the unspecified reserve protein comprising any number of concantenations; and maize seeds comprising said unspecified reserve proteins.

Applicant broadly claims an oligonucleotide comprising a concantenation coding for $(P-K)_n$ wherein 'n' is 2 or more, seeds of maize comprising an oligonucleotide comprising a concantenation coding for $(P-K)_n$ wherein 'n' is 2 or more, or a concantenation coding for (P-K) or K-$(P-K)_4$ or 2K$(P-K)_4$ either with or without intervening amino acids other than P or K; any plant reserve protein comprising modifications thereof; any maize reserve protein comprising modifications thereof; any maize zein protein comprising modifications thereof; any maize gamma zein protein comprising modifications thereof; any maize gamma zein preserve protein comprising modifications thereof wherein the oligonucleotide is inserted in place of or following a Pro-X domain naturally present in the gamma zein protein; and methods of increasing lysine in plants transformed therewith.

Applicant teaches increased lysine content in maize endosperm transformed with polynucleotides encoding 28kDa gamma zein from maize comprising high lysine modifications as P20γZ (SEQ ID NO: 11) having K-$(P-K)_4$ (SEQ ID NO: 3) inserted after the Pro-X domain,

H30γZ (SEQ ID NO: 7) having K-(P-K)$_4$ (SEQ ID NO: 3) replacing the Pro-X domain, and H45γZ (SEQ ID NO: 9) having K-(P-K)$_4$-E-F-K-(P-K)$_4$ (SEQ ID NO: 4) replacing the Pro-X domain (see pages 27-28 of the specification and Figure 3).

Applicant does not teach any other plants transformed with any other polynucleotides encoding a plant reserve protein having P-K concantenations for increased lysine other than maize transformed with polynucleotides encoding modified gaama (28 kDa) zein proteins.

Applicant asserts that the newly filed claims which have a basis in the previously rejected claims are now enabled (resposne page 20). Applicant has provided a conclusion that the claims are enabled but has not provided any evidence for enablement or any arguments directed towards the enablement art cited in the prosecution history. Moreover Applicant's assertions on page 21 that limiting the claims to maize seeds does not address the broad issue of describing and therefore enabling expression of a modified seed reserve protein. Furhter, enablement art was cited where a maize gamma zein was not expressed

Transformation of plants, maize or otherwise with non-endogenous reserve proteins either unmodified or modified to have increased lysine introduces an element of unpredictability. The inherent unpredictability in stable expression of either an unmodified or a modified reserve protein sequence is illustrated in an example where introduction of either form of a maize alpha zein reserve protein resulted in premature degradation in the seeds of transformed tobacco (Ohanti T. *et al.* Plant Molecular Biology, 1991, Vol. 16; pages 117-128; see Abstract) and in the example where insertion of pN13γZ having SEQ ID NO: 5 at 5 amino acid residues upstream of the carboxy terminus of the peptide resulted in no accumulation of gamma zein protein in transformed maize (Torrent M *et al.* 1997, Plant Molecular Biology, Vol. 34, pages 139-149; see

Abstract and pages 27-28 of the specification). Further, structural elements of 27 kDa gamma zein from maize are required for proper protein body assembly in maize endosperm indicating that there are required structural features for stable expression of reserve proteins in maize seeds (Coleman C. et al. The Plant Cell, Vol. 8; pp. 2335-2345; see page 2341 column 2 last paragraph to page 2342 column 1 line 8). Furthermore, see *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Given the unpredictability in the art for making or using DNA sequences encoding modified plant reserve proteins, comprising proline tandem rich repeats of unspecified length, number and identity, comprising any number of P-K concantenations that would stably express in a transformed plant; the breadth of the claims encompassing any plant transformed therewith; the lack of guidance in the examples of the specification or in the prior art as to which reserve proteins having proline rich tandem repeats, would when modified for high lysine express a stable protein in any host plant; and the undue trial and error experimentation required to practice the claimed invention, the invention is not enabled for the scope set forth in the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-43, 45-46, 84-123 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42 and 84 do not set an upper limit upon the size of the concantenation i.e. n = 3 or more; and as such the claim does not set forth the metes and bounds of the invention.

Claim 89 states that the oligonucleotide has the formula K-(P-K)$_4$ yet the claim from which Claim 89 depends states that the oligonucleotide has at least two concantenations of (P-K)$_n$ where n = 3 or more, which would require that at least 6 (P-K) units be present in the oligonucleotide and not 4 as set forth in Claim 89.

Regarding claims 42, 84, 110-111 and 114 and dependent claims 43, 45-46, 85-109, 112-113 and 115-123 the phrase "for example" and "in particular" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42-43, 45, 84-88 and 110-113 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 91/13991 published 19 September 1991.

WO 91/13991 teaches an isolated oligonucleotide encoding a polypeptide comprising at least two concantenations of $[P\text{-}K]_n$ where n is superior to 2, n is equal to 3 or more; and wherein neither P nor K residues separate at least one concantenation from a second concantenation in figure 4 see nucleotides 127 to 162 encoding amino acid sequence P-K-P-K-P-K-Q-E-A-M-P-K (see attachment #1 for marked up figure 4 for additional P-K concantenations); and thus the reference teaches all the limitations of Claims 42-43, 45, 84-88 and 110-113.

Claims 42-43, 45-46 and 84-123 are rejected.

Claims 46, 89, 114-124 are deemed free of the prior art given the failure of the prior art to teach or reasonably suggest plants transformed with polynucleotides encoding modified maize gamma zein (28 kDa) reserve proteins comprising concantenations of P-K and methods of expressing said proteins in a stable and functional manner in maize seeds.

Claim 124 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
May 15, 2006

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER